NRC Absorbed Dose Reconstruction for Family Member of ^{131}I Therapy Patient: Case Study and Commentary

A patient with terminal metastatic thyroid cancer and severe renal insufficiency was treated with 10,545 MBq (285 mCi) $Na^{131}I$ and hospitalized in accordance with Nuclear Regulatory Commission (NRC) requirements pursuant to 10 Code of Federal Regulations (CFR) Part 35.75. The patient died while still in the hospital, 6 days after radiopharmaceutical administration. The radiation safety officer (RSO) measured radiation levels in the patient's room each day, both at 1 m from the patient and at the patient's bedside. The initial dose rate measurements after radiopharmaceutical administration were 0.040 cSv/h (rem/h) and 0.400 cSv/h (rem/h) at 1 m and at the bedside, respectively. According to the NRC, these radiation levels diminished with an effective half-time of 3 to 4 days.

A close adult relative of the patient disregarded the instructions of the RSO and insisted on staying close to the patient for long periods of time until the patient's death. The relative was reminded by licensee staff, including the RSO, to take a position behind a bedside shield. As a result of the relative's proximity to the patient and the amount of time spent in areas of elevated radiation levels, the licensee later reported to the NRC that the relative probably received a dose in excess of the 1 mSv (100 mrem) regulatory limit.

The NRC subsequently performed a dose reconstruction using the RSO's measured dose rate values at the bedside and the daily stay times for the relative that were determined from interviews with the relative and licensee staff. Details of this analysis are publicly available in NRC's Agencywide Documents Access and Management System (ADAMS; www.nrc.gov/reading-rm/adams.html; search for accession number ML023440102). NRC determined the total effective dose equivalent (TEDE) by multiplying the measured dose rates by the relative's stated stay times. The dose rates, stay times, estimated TEDE during each day, and the total TEDE are presented in Table 1, where the TEDE is estimated to be 15 cSv (rem) for the relative. Only the external dose component was considered. No mention was made of the possibility or likelihood of internal intake. Therefore, the TEDE is equal to the deep dose equivalent (DDE).

SNM and ACNP Concern Over NRC Dose Reconstruction

The SNM and the American College of Nuclear Physicians (ACNP) were concerned that the NRC's dose reconstruction in this case might be overly conservative. Meetings with NRC Commissioners Edward McGaffigan, Jr., and Jeffrey S. Merrifield were held to discuss NRC dose reconstructions as well as to suggest the formation of an independent committee composed of experts from the SNM and ACNP and other dosimetry experts to conduct peer reviews of NRC dose calculations. On September 9, 2003, NRC Chair Nils J. Diaz sent a letter to Henry Royal, MD, SNM president, making the following statements of interest:

> In this particular case, the hospital had performed daily dose rate measurements at the bedside. The NRC estimated the stay times next to the bed based on interviews with the [relative] and the hospital staff. The dose to the [relative] was then calculated using these stay times and

From the Newsline editor:

Newsline welcomes discussion on important practice issues in nuclear medicine. This month, we present commentary on absorbed dose reconstruction from 2 SNM members with a wealth of practical and published experience. Because the material pertains to Nuclear Regulatory Commission (NRC) actions in a specific case study, NRC representatives were given an opportunity to respond and have indicated their intention to do so in a subsequent issue of Newsline. Ties between the NRC and the nuclear medicine community go back more than a half century. Frank and open discussion of points of difference is likely to extend the benefits of this working relationship well into the future.

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Editor, JNM Newsline

TABLE 1
Bedside Dose Rates, Stay Times, and NRC TEDE Calculations

Day	Dose rate at bedside (cSv/h or rem/h)	Stay time (h)	TEDE (cSv or rem)
0	0.400	0	0
1	0.348	6	2.088
2	0.250	12	3.000
3	0.210	12	2.520
4 (through 5 PM)	0.210	8.5	1.785
4 (5 PM–midnight)	0.210	7	1.470
5	0.132	20.5	2.706
6	0.107	11.5	1.231
			Total 14.800

the measured exposure rate for each day. Since the NRC staff was able to use measured dose rates and did not have to perform a complex dose reconstruction analysis, the Commission does not feel that the staff's results were overly conservative. . . .

While we appreciate your offer to have an independent SNM/ACNP Committee review our calculations, we believe the staff gets sufficient support from its existing medical and scientific consultants, contractors, and the ACMUI [Advisory Committee on Medical Uses of Isotopes] in performing and reviewing its dose reconstructions. . . .

The staff will also continue to evaluate the state of the art in dose reconstruction in order to keep its determinations as realistic as possible.

The NRC thus maintains that its dose reconstruction in this case is not overly conservative and suggests in the final sentence quoted here that its methods and results were as realistic as possible. However, the NRC appears to have been constrained by their methods and licensee-supplied data. We will present here an alternative dose reconstruction taking into account the many uncertainties in this case and using more robust assumptions and calculation methods.

Alternative Dose Reconstruction

The initial dose rate measurement at 1 m from the patient was 0.040 cSv/h (rem/h). The reasonableness of this measurement can be ascertained by theoretical calculation:

$$\text{Dose rate at 1 m (cSv/h)} = \Gamma \times A_0 \times SF,$$

where Γ = specific γ-ray constant for ^{131}I at 1 m, 5.95E-6 cSv-m^2/MBq-h; A_0 = 10,545 MBq; and SF = shielding factor resulting from patient attenuation. For ^{131}I this has been reported to be 0.6, on average (*1*). Thus, dose rate at 1 m = 5.95E-6 × 10,545 × 0.6 = 0.038 cSv/h.

According to this theoretical calculation, the 0.040 cSv/h measurement at 1 m is therefore realistic and reasonable. (Note: This simple calculation illustrates that even if no dose rate measurements had been obtained, no "complex dose reconstruction analysis" would have been needed.)

No such theoretical calculation can be used to directly verify the initial 0.400-cSv/h dose rate measurement at the patient's bedside, because no distance was given. The NRC did not attempt to estimate this distance and apparently assumed that the relative's location corresponded to dose-rate levels measured at the patient's bedside. The NRC was told by the relative that when in the room the bedside distance was maintained; however, "bedside" is imprecise and not a standard unit of length. We believe that it is imperative to **reconstruct the distance before reconstructing the dose.** The initial measured dose rate at 1 m can be used to estimate the distance at which the bedside dose-rate measurements were taken. Using the inverse square law ($^{40}/_{400}{}^{1/2}$), the bedside dose rate is estimated to be at a distance of 31.6 cm from the patient. Because this initial dose-rate measurement was performed at a time when the activity was mainly confined to the stomach, a point source assumption and use of inverse square is an adequate approximation. Does 31.6 cm realistically represent the distance between the relative and the patient? If not, the bedside dose-rate measurements cannot be used to estimate the relative's exposure.

From the NRC's dose reconstruction in the ADAMS document, it is reported that the relative's closest position to the patient was sitting against the bed, with elbows or forearms on the bed. The NRC approach to dose calculation is precisely defined in 10 CFR Part 20. Pursuant to 10 CFR 20.1003, portions of the arms distal to and including the elbows and portions of the legs distal to and including the knees, as well as hands and feet, are extremities. Doses to extremities are reported as shallow dose equivalents. For purposes of external exposure, the head and trunk and the arms and legs proximal to elbows and knees, respectively, are considered "whole body parts" for which DDEs are calculated. Because the TEDE in this case is equivalent to the DDE and, pursuant to 10 CFR 20.1201(c) the assigned DDE must be for the part of the body receiving the highest exposure, we first assumed that the relative's proximal arms were at the closest distance to the patient and therefore received the highest exposure. It is reasonable to assume that this patient-to-relative's proximal arm distance could be on the order of 31.6 cm. If the relative's proximal arms remained in this position for the entire stay times (as stated by the relative), then the bedside dose rates used by NRC to estimate TEDE are a reasonable approach for regulatory purposes.

However, based on human experience, some follow-up questions of the relative might have led to an alternate dose reconstruction scenario. It is likely that the relative's body, including proximal arms, was at a greater distance for some of the time, as a result of changing positions for comfort during prolonged stay times. For example, it is likely that the relative sat back in the chair at least part of the time, instead of being continually hunched forward over the bed. It is not unlikely that this comfort distance could be around 1 m, while still being "at bedside." It is therefore reasonable to assume, even in light of the relative's statements, that the relative's closest

distance was at an average "bedside" distance between 31.6 and 100 cm (i.e., an average distance of 65.8 cm). That is, the proximal forearm averaged a distance of 65.8 cm from the patient. **In this case, the NRC dose estimate is overly conservative by a factor of $(65.8/31.6)^2$ or 4.3.**

To this point, we have used NRC regulatory definitions and criteria for the TEDE calculation (i.e., the dose to the proximal arm has been the point of evaluation as is necessary for any regulatory assessment). The TEDE can also be determined in this case for the relative's trunk as the surrogate for "whole body" TEDE. Although this approach is not specifically addressed in NRC regulations, we believe it would be prudent to determine this additional dose estimate, especially in this case in which the proximal arms and trunk of the body were at significantly different distances from the patient. Thus, if TEDE values are to be used in a risk assessment, it may be important to differentiate the estimated dose values for the individual's arms from those of the trunk. A TEDE value to determine whether a violation of NRC regulations occurred and a TEDE value most appropriate for risk assessment are not necessarily the same.

Simulated measurements of the patient–relative geometry performed independently by the authors yielded a center-of-gravity to center-of-gravity (umbilicus-to-umbilicus) distance of 65–70 cm. On average, the umbilicus-to-umbilicus distance, therefore, was between 65 and 100 cm, for an average distance of 82.5 cm. **Using this scenario, the NRC dose estimate is overly conservative by a factor of $(82.5/31.6)^2$ or 6.8 using the relative's trunk as the whole body part of interest.**

Another important factor to consider is attenuation by the exposed individual's body. The NRC has taken into account shielding by the patient's body by using a measurement instead of using the specific γ-ray constant for an unshielded point source. However, the NRC did not take into account the shielding (i.e., attenuation) by the body of the family member, which requires essentially the same shielding factor as that which applies to the patient. The TEDE is not equivalent to the dose rate multiplied by time; the attenuation by the exposed individual must be taken into account. For ^{131}I, the shielding factor is, on average, 0.6 for the patient, as previously discussed (*1*), and also 0.6 for the family member's body (*2*). The attenuation factor for the DDE, according to NRC regulation, however, is different. According to 10 CFR 20.1003, the DDE, ". . .which applies to whole body exposure, is the dose equivalent at a tissue depth of 1 cm. . . ." Using the linear attenuation coefficient for ^{131}I in tissue-equivalent material (*4*) and a depth of 1 cm, the corresponding attenuation factor for the DDE is $e^{-(0.11)(1)}$ or 0.9. **Thus, the NRC overestimated the relative's TEDE, based on its own regulatory criteria, by an additional factor of 1/0.9 or 1.1 based on use of the proximal arm. The TEDE overestimate is 1/0.6 or 1.7 based on the use of the trunk of the body.**

The NRC's dose reconstruction also did not take into account several other important factors. The NRC assumed that the exposure rate at a single point in time measured by the RSO was constant for 24 hours, instead of exponentially decreasing. Although it is reasonable to ignore decay if the effective half-time is long, in this case it was only 3.1 days, based on the time–bedside dose rate data. In addition, there is an obvious mistake in the dose rate on day 4, which cannot be the same as it was on day 3 (Table 1). Finally, at times shortly after dose administration, this patient is not really a point source but more closely resembles a line source (*3*). This is especially important at short distances from the patient, because it decreases the exposure relative to that which is calculated using the inverse square law. **These 3 considerations taken together potentially represent an additional NRC dose overestimate by a factor of 1.5.**

Thus, the NRC's dose calculation is conservative by a factor of only 1 × 1.1 × 1.5 or 1.6 using the proximal arms as the body part receiving the highest exposure under the assumption that the proximal arms are always at a distance of 31.6 cm from the patient. If the proximal arms are at an average distance of 65.8 cm, the NRC calculation is conservative by a factor of 4.3 × 1.1 × 1.5 or 7.1. If umbilicus-to-umbilicus calculations are used, the NRC dose calculation is potentially overly conservative by a factor on the order of 6.8 × 1.7 × 1.5 or 17. The relative's TEDE may well be a maximum of only 0.9 cSv if umbilicus-to-umbilicus calculations are used.

CONCLUSION

A specific dose reconstruction performed by the NRC has been reported. An analysis of the NRC's dose reconstruction methods indicates a potential dose estimate that is overly conservative by a factor of approximately 1.6, 7.1, or 17, depending upon calculation methods and assumptions. NRC regulations require that the TEDE be calculated for the body part receiving the highest external exposure at a tissue depth of 1 cm. Nothing in the regulations, however, precludes the additional use of other body parts and/or shielding factors, as may be appropriate, for the TEDE calculation. We believe that the factor of 17 realistically applies to the true whole-body dose in this case and that the factors of 1.6 and 7.1 more accurately reflect the proximal arm dose. If a dose estimate is to be used to determine risk, as the NRC did in this case, then we recommend use of not only the regulatory-mandated TEDE value but also the most appropriate TEDE value based on the specific circumstances.

We recognize that "state-of-the-art" dose reconstruction should result in a probability distribution rather than a single dose estimate. The uncertainty for each parameter in the calculation should be modeled, and Monte Carlo simulation could then be used to get a frequency distribution

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derwent combined chemo- and radiotherapy. In a third patient, no sentinel node was identified. The authors concluded that, "Laparoscopic detection of sentinel nodes using ^{99m}Tc-labeled colloid is feasible in patients with primary and recurrent vaginal cancer and may provide important information to direct further management."

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of the likely dose. This, however, is beyond the scope of this case report.

All licensees should expect the NRC to perform dose calculations using state-of-the-art dosimetry methods that result in realistic and not overly conservative dose estimates. This is especially important because these dose estimates are used for risk assessment. The large discrepancies in methodology, criteria used, and estimated dose demonstrated in this case raise important issues. We therefore recommend that the NRC Commissioners consider a case-by-case review of staff dose calculations by an outside expert panel to gain valuable perspectives and appropriate calculation strategies to assure that these dose estimates are realistic and represent values that not only comply with regulatory requirements but also can be used for appropriate risk assessment.

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at Camp David that would result in an accord between Egypt and Israel. Attendees at our meeting were fascinated by glimpses of Senator Ted Kennedy, Israel's Prime Minister Menachem Begin, and other dignitaries passing through the hotel lobby.

As would be expected from a meeting in the nation's capital, the opening ceremony included a letter from President Jimmy Carter and talks by Nobel laureate Rosalyn Yalow and Donald Frederickson, director of the National Institutes of Health. On September 18, the Preservation Jazz band gave a special Kennedy Center concert for the attendees, followed by a rooftop reception. On September 20, the National Gallery of Art opened its doors for a private showing, with a performance by the National Gallery Orchestra.

The meeting was an overwhelming success and was greatly rewarding for attendees, individuals presenting scientific papers, and the dedicated organizers, which, in addition to those mentioned already, included: Anne Wagner and Arlene Reba, who chaired the Social Program Committee; Cecil Barrett, the Hilton employee who "made the trains run on time" throughout the meeting; and Beatrice Smith, who kept detailed minutes during the planning.

Is It Not Time Again?

An important question is whether it is time again for the United States to host the World Congress of the WFNMB. Six years before the date of each Congress, the WFNMB assembly meets to choose a host city. Should the SNM submit a proposal to the assembly for the meeting to be held in the United States in 2014? At that time, 36 years will have passed since the meeting in Washington in 1978. Some believe that the World Congresses of the WFNMB should be held only in developing countries. Others believe that, with respect to nuclear medicine, we are all developing countries and that the goals of the Second World Congress are as worthy today as they were in 1975.

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